Aldehyde Functionalized Cellulose Support for Hydrogels

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ABSTRACT: Activated cellulose carrying aldehyde (CHO) and acylchloride (COCl) reactive sites was created by reacting cellulose with dialdehydes, i.e., polyethylene glycol (PEG) diacylchloride and glutaraldehyde (GA), to yield Cell-PEG-COCl and Cell-CHO, respectively. Cellulose fibers and microcrystalline cellulose were readily esterified by PEG diacylchloride to form Cell-PEG-COCl to reach as high as 0.24 to 0.37 mmol aceylchloride per gram cellulose, respectively. The generation of free COOH from PEG diacylchloride reactions was optimized at the lower COCl/OH ratio, where the tendency to half-ester formation was more prevalent than to diesters. Reactions with 8 and 16% GA, generated 0.83 to 1.26 μmol free aldehyde per gram of cellulose, respectively. The reactivity of the aldehyde groups toward poly(vinyl alcohol) (PVA) hydroxyl was robust, generating cellulose fiber supported PVA hydrogels that could swell up to 62 times. These reactions have shown to be highly effective to create aldehyde functionalized cellulose and demonstrated a simple, yet viable way to support PVA hydrogels for superior swelling and improved mechanical stability. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 118: 2489–2495, 2010

Key words: cellulose; surface functionalization; glutaraldehyde; diacylchloride polyethylene glycol

INTRODUCTION

Cellulose is the most abundant naturally occurring polymer and its chemical reactions continue to be the predominant route toward achieving diversified functional properties and advanced material applications. The most prevalent reactions involve, the primary hydroxyl at C-6 atoms and two secondary hydroxyls at C-2 and C-3 of the β-1,4-anhydroglucopyranose repeating unit of cellulose via esterification and etherification. For instance, conversion of these hydroxyl groups to cellulose derivatives with methyl, ethyl, amino ethyl, and acetate groups have been extensively explored to fabricate membranes as artificial kidneys, encapsulating materials for controlled drug delivery, sutures and bandages, and blood compatible biomaterials.[1]

Polyfunctional agents capable of reacting with hydroxyl groups, such as dialdehdyes including glutaraldehyde (GA) and glyoxal, have shown to be effective nonformaldehdye durable press finishes to improve the dimensional stability and wrinkle resistance of cotton fabrics.[2,3] Grafting on cellulose fiber surfaces is a common approach to generate new material properties and have been reported widely. We have introduced carbon-carbon double bond (C=C) to cellulose fiber surfaces via either enzyme-catalyzed transesterification with vinyl ester[4] and esterification with methacrylate chloride.[5] A highly efficient procedure has been devised to regioselectively introduce vinyl esters (propionate and acrylate) on the C6 hydroxyl of cellulose via enzyme-catalyzed transesterification to allow further graft polymerization.[4] The surfaces of electrospun cellulose fibers (100–450 nm) have also been functionalized with methacrylate chloride to enable graft copolymerization with methyl methacrylate, acrylamide, and N-isopropylacrylamide through the incorporated C=C groups.[5] In another study, electrospun cellulose fibers (500 nm diameter) were reacted with polyethylene glycol (PEG) diacylchloride to tether enzymes.[6] The PEG spacers not only improved the catalytic activity of fiber-bound lipase by 10 fold at a significantly higher elevated temperature of 70°C but also retained superior catalytic activity following exposure to several organic solvents.

In the present study, two homo-difunctional compounds, i.e., diacylchloride containing PEG and GA, are explored to introduce reactive aldehyde and acylchloride sites to cellulose fibers and microcrystalline cellulose (MC) powders. Both GA and PEG have biological and biomedical significance. GA has been used extensively for fixation of cells, immobilization of enzymes, and crosslinking of proteins and polysaccharides for controlled release applications.[7,8] Grafting PEG to polymers has been a widely

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accepted approach to impart polymer surfaces biocompatibility as well as protein rejection.[9] The reactivity of the aldehyde on the GA activated cellulose is verified by reactions with amine and hydroxyl-containing compounds. Specifically, the aldehyde carrying cellulose surfaces were explored to support the direct formation of poly(vinyl alcohol) (PVA) hydrogels without using any crosslinking agents, demonstrating the potential of single-step hydrogel formation from other polymers on activated cellulose fiber supports.

EXPERIMENTAL

Materials

Microcrystalline cellulose (MC, ~ 20 μm, Aldrich, St. Louis, MO) powder and cellulose fiber (Whatman 3 filter paper, Fisher, Waltham, MA) were used as the cellulose solids for the study. Aluminum sulfate ($Al_2(SO_4)_3$) $18H_2O$ and PVA (M_w 124,000–186,000, 87–89% hydrolyzed) were obtained from Aldrich. Poly(ethylene glycol) bis(carboxylic acid) (HOOC—PEG—COOH, MW = 600 Dalton, Acros), thionyl chloride ($SOCl_2$, Aldrich, 99%), toluene (Fisher) and pyridine (Acros, Geel, Belgium) were used as received. Aqueous glutaraldehyde solution (GA, 50%), *o*-nitrophenol (99%), silver oxide, 3-methyl-2-benzothiazolone hydrazone hydrochloride (MBTH), ferric chloride ($FeCl_3$, 98%), *p*-amino benzoic acid (PABA, 99%), and phenyl-ethylamine (PEA, 99%) were supplied by Acros. Purified water Milli-Q plus water purification system (Millipore, Billirica, MA) was used to prepare all aqueous solutions.

Polyethylene glycol (PEG) diacylchloride activated cellulose

The carboxylic end groups on the poly(ethylene glycol) bis(carboxylic acid) (PEG11) were acylated by reacting 10 g with 8 mL $SOCl_2$ under N_2 purge at ambient temperature overnight. Cellulose filter paper and MC powder were dried at 80°C, and immersed in 1 : 1 toluene: pyridine mixtures containing the acylated HOOC—PEG—COOH or ClOC—PEG—COCl. The reactions were carried out under constant stirring and N_2 purge at ambient temperature for 2 days. The PEG-modified cellulose filter paper and MC powder were washed by hot methanol completely, dried at 80°C for characterization. The modified filter paper and MC powder were referred as PEG11-FP and PEG11-MC, respectively, followed by an additional number denoting the amount of PEG.

The total quantity of free acid COOH and ester OCO of the modified cellulose was quantified by saponification.[10] The saponification value was determined by hydrolysis of the esterified materials with 0.1N NaOH at ambient temperature overnight and subsequent determination of the excess NaOH by titration with 0.1N HCl to the phenolphthalein end point. The total quantity of free acid and ester was estimated by the difference between total and excess NaOH. The free acid content was determined by the extent of reaction with silver *o*-nitrophenolate. The esterified cellulose samples were shaken in a saturated aqueous solution of silver *o*-nitrophenolate for two days. The amount of silver consumed was determined by potentiometric titration of an aliquot of the solution against 0.02N HCl to a pH of 4.6.

GA-activated cellulose (cell-CHO) fibers

Cellulose fibers were reacted with GA at 2, 4, 8, and 16% (w/v) concentrations and were referred as GA-FP-2, GA-FP-4, GA-FP-8, and GA-FP-16, respectively. The cellulose fibers were impregnated in the GA solutions for 10 min, then drying at 80°C for 3 min. A Lewis acid, aluminum sulfate $Al_2(SO_4)_3$ (AS) was added as the catalyst and its effects were studied by varying AS:GA from 0.01 : 1 to 0.03 : 1 ratio at a constant 8% GA. The dried fibers were then cured by heating at varying temperatures from 120°C to 140°C for 3 min as well as for different lengths of time between 3 and 6 min at 120°C. After curing, GA treated cellulose fibers were washed with water (described in the next section) and dried at 80°C for further characterization and functionalization.

The unreacted GA released from cured GA-treated cellulose into the water rinse was monitored over time by reacting MBTH with GA and quantified.[11] Briefly, the GA aldehyde groups react with MBTH to form azine, which is oxidized by reactive cation to yield a blue cation that in acetone, exhibits maximum absorption at 663 nm wavelength. Weighed GA-treated cellulose was immersed into 300 mL deionized water at ambient temperature. 0.3 mL of the extraction solution was sampled at selected time intervals between 0.5 and 24 h, and mixed with an equal volume of 0.4 wt % MBTH solution. After 30 min, 1.5 mL of 0.2 wt % $FeCl_3$ was added and, after 5 min 3.9 mL acetone was added and allowed to stand for 5 min. The absorbance at 663 nm was measured by a UV–vis spectrophotometer (Hitachi U-2000) and converted to GA concentrations in the extraction using a calibration curve obtained from GA solutions of known concentrations.

The free aldehyde groups on the GA-activated cellulose was quantified by reacting with the amine of PABA[12] and measured by UV–vis spectroscopy at a wavelength of 265 nm. The quantity of the aldehyde groups on the GA-activated cellulose was derived by the calibration established by the same reaction

with known GA quantities in 2–20 mg/L concentration range, Abs = 0.0832 x Conc (mg/L) at r^2 = 0.9881.

PVA hydrogels supported on GA-activated cellulose fibers (cellulose-CHO)

Cellulose fiber supported PVA hydrogels were formed by reacting cellulose-CHO fibers with aqueous PVA solution (2%, w/w) at 25°C and 37°C under pH 3.0. Cellulose-CHO fibers, prepared from reaction with 8% GA at 0.02 AS:GA ratio and cured at 120°C for 3 min, were used. The obtained cellulose supported hydrogels were washed by deionized water for further characterization. For comparison, PVA-GA hydrogels were also prepared by reacting aqueous PVA solution (2%, w/w) with GA at varying OH/CHO ratios between 0.4 and 60, pH from 1.5 to 4, and temperatures between 25 and 50°C.

Cellulose fiber supported PVA hydrogels were reimmersed into water to fully swell to get wet weight (W_w). Swollen cellulose-hydrogels were then dried at 80°C until reaching constant dried weights (W_d). The swelling degree (SD) of cellulose-hydrogels was calculated as: SD = $(W_w - W_d)/W_d$. The same characterization was conducted on the PVA-GA hydrogels.

FTIR spectroscopy and thermal analysis

GA solutions with different concentrations were characterized by FTIR using NaCl plates. Chemical structures of cellulose, activated cellulose with GA and PEG diacylchlroide, and products from reactions of cellulose-CHO with PEA were identified by KBr-FTIR (Nicolet Magna IR 560) from 4000 to 500 cm^{-1} at a resolution of 4 cm^{-1}. Thermal properties of cellulose and modified cellulose were measured by differential scanning calorimetry (Shimadzu DSC 50) and thermogravimetric analysis (Shimadzu TGA-50) from ambient temperature to 500°C at 10°C/min under N_2 atmosphere.

RESULTS AND DISCUSSION

PEG diacylchlride reaction with cellulose

Both cellulose fibers and microcrystalline (MC) cellulose powder were reacted with 600 Da PEG diacylchloride, referred to as PEG11. The FTIR spectrum of cellulose fibers reacted at a constant 8 COCl/OH ratio (PEG11-FP-8) showed two new weak peaks at 1711 cm^{-1} and 1767 cm^{-1}, likely from the formed ester linkages (OCO) between cellulose and PEG, as well as free COCl groups [Fig. 1(a)]. Four other peaks at 1163, 1112, 1059, and 1031 cm^{-1} also appeared and could be attributed to the ether bonds (CH_2—O—CH_2) of the PEG chains. Titration of the hydrolyzed PEG-modified fibers in aqueous media gave 0.24 mmol and 1.68 mmol of free COOH and OCO/COOH per g cellulose, respectively. The free COOH attained was 14% of the total OCO/COOH.

The MC powders were reacted with PEG11 at 0.5, 1, 2, and 20 COCl/OH molar ratios and referred as PEG11-MC-0.5, PEG11-MC-1, PEG11-MC-2, and PEG11-MC-20, respectively. FTIR spectrum of all PEG-modified MC powders showed C=O stretching peak at 1750 cm^{-1} [Fig. 1(b)]. Peak intensity of the carbonyl stretching remained similar on the PEG11

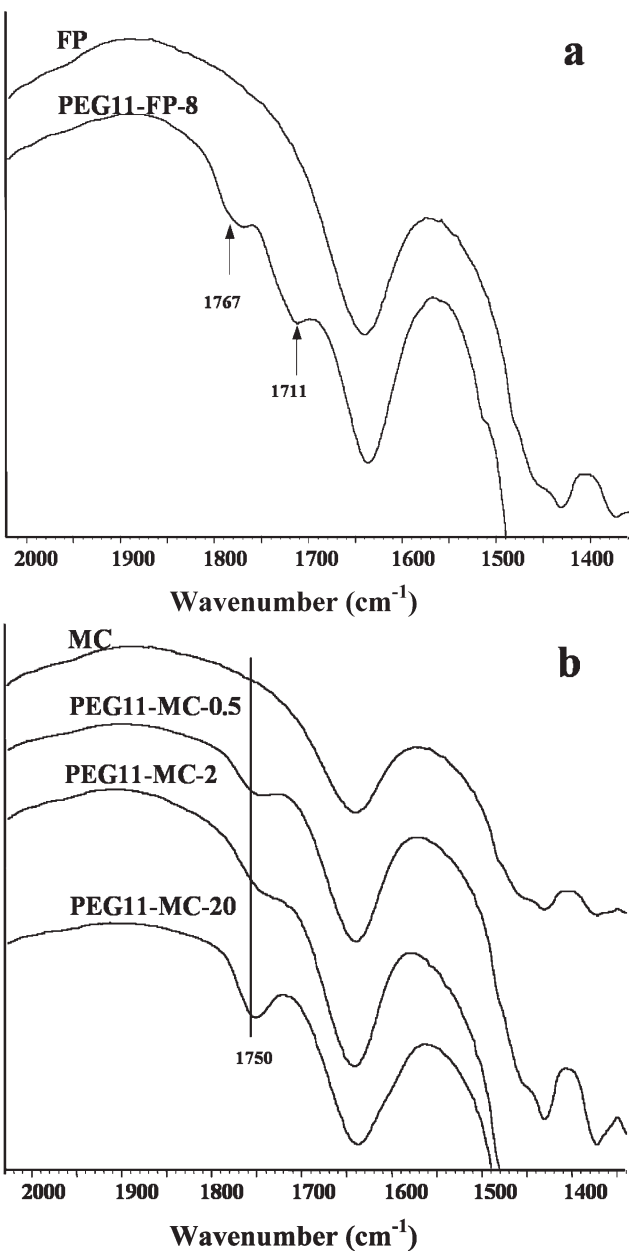


Figure 1 FTIR spectra of PEG attached cellulose with PEG diacylchloride of MW 600: (a) PEG11-FP-8 fibers (COCl/OH of 8); (b) PEG11-MC powders at varying COCl/OH ratios between 0.5 and 20.

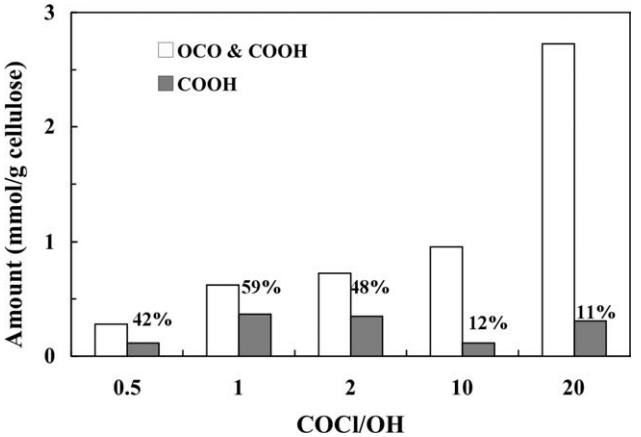
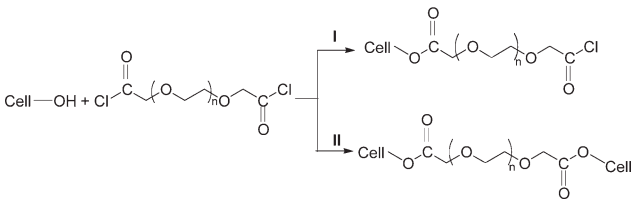


Figure 2 Amounts of (□) OCO and COOH, and (■) COOH groups on PEG11-MC at varying COCl/OH ratios between 0.5 and 20 with PEG diacylchloride MW of 600.

modified MC at lower COCl/OH ratios, but was significantly higher on one reacted at the 20 COCl/OH ratio. The combined OCO and COOH increased from 0.3 to 0.6 and 0.7 mmol/g cellulose with increasing COCl/OH from 0.5 to 1 and 2, respectively, and reached 2.7 mmol/g cellulose at 20 COCl/OH (Fig. 2). The significantly higher combined OCO/COOH at 20 COCl/OH is consistent with the much intensified C=O peak observed on PEG11-MC-20. The free COOH also increased from 0.12 mmol/g cellulose at 0.5 COCl/OH to 0.37 mmol/g of cellulose at 1 COCl/OH ratios, then slightly reduced to 0.35 mmol/g of cellulose at 2 COCl/OH, lowered further to 0.31 mmole/g cellulose at 20 COCl/OH. Overall, the fractions of COOH over the combined OCO/COOH were 0.4, 0.62, 0.5, and 0.12 at COCl/OH ratios of 0.5, 1, 2, and 20, respectively. Therefore, the optimal free COOH of 0.37 mmol/g cellulose, or 62% of total OCO and COOH, was reached at 1 COCl/OH ratio.

The free COOH generation of 0.37 mmol/g cellulose on the MC powder is higher than the 0.24 mmol/g or 14% of total OCO and COOH achieved on the paper cellulose fibers. However, neither was as high as the 1.0 mmol of COOH/g of cellulose on the electrospun cellulose fibers that had much higher specific surface and likely less ordered cellulose structure.[6]

The esterification reactions between cellulose and PEG-diacylchloride can lead to the formation of either cellulose diesters or acidic cellulose half-esters (**S**cheme 1). Reaction of only one of acylchloride groups leads to the formation of acidic half-esters of cellulose (pathway I), whereas esterification of both acylchloride groups produces intermolecular and/or intramolecular crosslinked cellulose diesters (pathway II). From the quantity of the free COOH and the proportion of COOH over the total OCO/COOH acquired, the reaction of cellulose with PEG-diacylchloride were more efficient on the MC powders than cellulose fibers filter paper. Furthermore, the generation of free COOH was optimized at the lower COCl/OH ratio, where the tendency of forming half-esters (pathway I) appeared higher than diesters.



Scheme 1 Reactions between cellulose and PEG-diacylchloride.

GA-activated cellulose (cell-CHO) fibers

In reacting GA with cellulose fibers, the amounts of GA released from GA-activated cellulose fibers into water over time were measured (Fig. 3). At 0.5 h, the GA released from reactions with 2, 4, 8, and 16% of GA was 109, 148, 227, and 588 μmol/g cellulose, respectively. The GA released was significantly lowered after 1 h to 21, 42, 37, and 93 μmol/g cellulose and remained at similarly low levels over time regardless of GA concentrations employed. After 24 h, GA was not detected in any of the aqueous solutions except for that containing cellulose reacted with 16% GA, showing 20 μmol per/g cellulose. To remove residual GA efficiently, particularly necessary for reactions at high concentrations, the rinsing procedure was modified to changing the rinse every 5 min during the first 0.5 h then every hour thereafter under constant stirring. Monitoring of GA concentrations of the rinses showed complete removal

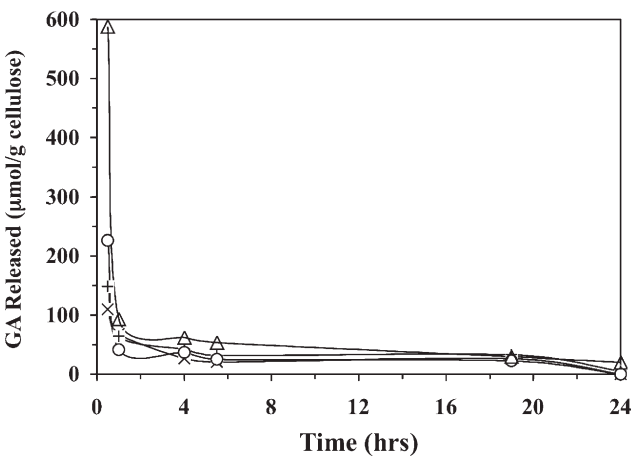


Figure 3 GA released from activated cellulose fibers with (×) 2, (+) 4, (○) 8, and (Δ) 16% GA solutions (AS : GA = 0.02 : 1, 10 min immersion, dried at 80°C for 3 min, cured at 120°C for 3 min).

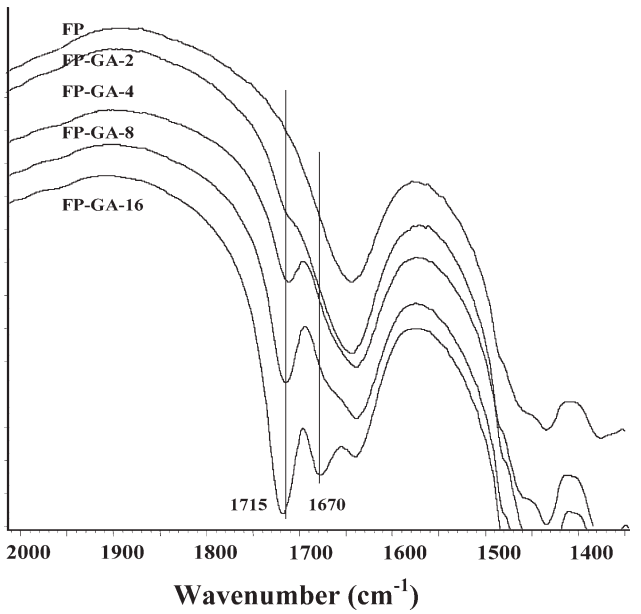
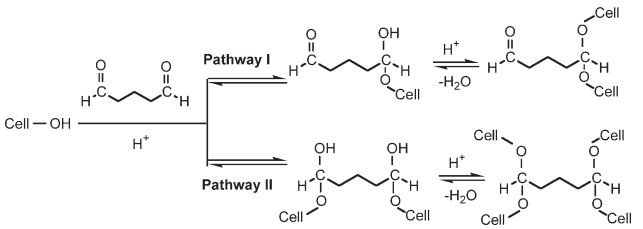


Figure 4 FTIR spectra of GA-modified cellulose fibers at different GA concentrations (AS:GA = 0.02:1, 10 min immersion, dried at 80°C for 3 min, cured at 120°C for 3 min).

of residual GA took 24 h or 30 rinse cycles. Therefore, all GA-activated cellulose fibers were washed by this modified manner described above and considered "GA-free".

The FTIR spectrum of GA-activated cellulose fibers showed a clear carbonyl (C=O) stretching peak at 1715 cm^{-1} (Fig. 4). The carbonyl peak intensified with increasing GA concentrations from 2 to 16%. Another peak at 1670 cm^{-1} was clearly observed on cellulose activated with 16% GA, but appeared as a weak shoulder on fibers modified with 8% GA. This band at 1670 cm^{-1} is believed to be from the C=C double bond of the reaction products with other coexisting forms of GA, a subject to be discussed later. Cellulose fibers were also reacted with 8% GA at varied amount of aluminum sulfate catalyst and curing times. No observable change was made on the C=O peak at 1715 cm^{-1}, although the 1670 cm^{-1} peak intensified slightly with increasing curing time from 3 to 5 min as well as increasing catalyst amounts, i.e., AS : GA from 0.01 : 1 to 0.03 : 1 (data not shown).

Reaction between an aldehyde and cellulose involves the reversible reaction of intermolecular acetal formation.[10,11] The reactions between GA and cellulose, however, are much more complicated than a simple acetal formation (**S**cheme 2). This is because of the different coexisting forms of GA in aqueous solutions, i.e., hemihydrate, dihydrate, and cis and transisomers of cyclic hemiacetal, as well as dimers and acetal-like polymer structures (**S**cheme 3). The free form of GA has been reported to account

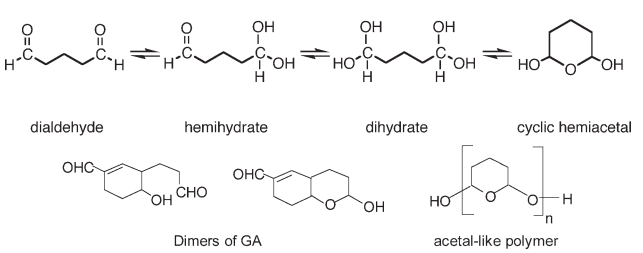


Scheme 2 Possible reactions between GA and cellulose.

for only a very small portion in the mixtures, i.e., about 4% of this equilibrium at 23°C.[13] In fact, FTIR of GA solutions showed that only the 50% concentration stock solution exhibit a clear aldehyde carbonyl peak (Fig. 5). The aldehyde stretching appeared as weak shoulder peaks in the spectra of 16 and 8% GA solutions, whereas none was observed in that of 2 and 4% GA solutions. It is, therefore, reasonable to expect that several coexisting forms of GA may react with cellulose simultaneously to give different products.

The 1715 cm^{-1} peak observed on the GA-activated cellulose gave evidence to the presence of carbonyl groups, indicating reaction products formed via Pathway I as illustrated in Scheme 2. The relatively low peak intensity may reflect the limited spatial availability of hydroxyl groups on the cellulose fibers that are relatively crystalline. The 1670 cm^{-1} peak observed on some of GA-activated cellulose may be because of C=C stretching resulted from reactions with C=C—bearing GA dimers (**S**cheme 3). This suggests that the formation of dimers and their reactions with cellulose may be favored under extended reaction conditions, i.e., higher GA and AS concentrations, higher temperatures and longer time. Depending on the dimer structures, such reactions may or may not introduce aldehyde functionality on the cellulose. This information provides insights into strategies to control undesirable reactions. The 8% GA at moderate reaction conditions appeared to produce abundant aldehyde functionality with minimal products from reacting with other coexisting forms of GA.

The presence of aldehyde on the modified cellulose was further quantified by reaction with PABA, where the PABA amine (NH_2) reacts only with the free aldehyde. The quantities of free aldehyde on the



Scheme 3 Different forms of GA in aqueous solutions.

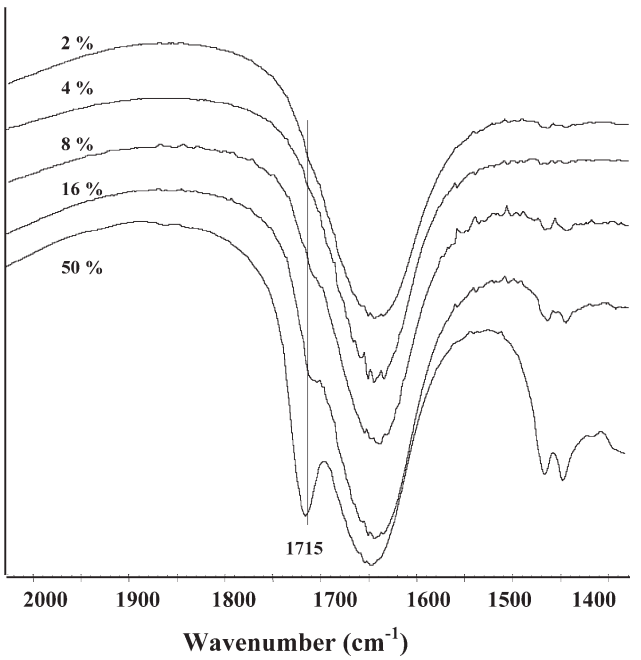


Figure 5 FTIR spectra of aqueous GA solutions of 2–16% concentration.

cellulose fibers reacted with 8 and 16% GA were 0.83 and 1.26 μmol/g cellulose, respectively, but were not detected on those reacted with either 2 or 4% GA. Quantification by the reaction with PABA, coupled with the FTIR spectra give clear evidence that aldehyde groups are introduced by reactions with GA at 8% or higher to give rise to cellulose-CHO. The ability of the GA-activated cellulose fibers, or cellulose-CHO, to be functionalized was studied further as follows.

PVA hydrogels on GA-activated cellulose fibers

The GA-activated (8% GA at 0.02 AS:GA ratio, 120°C, 3 min) cellulose fibers were used to react with PVA to generate hydrogels on fiber surfaces. The reactions were conducted under different conditions of OH/CHO ratios (0.4–58), pH values (1.5–10) and temperatures (25–50°C). The SD of the gels formed was measured to find the optimal gel formation condition. Raising OH/CHO ratios from 0.4 to 58 significantly increased the SD of PVA-GA gels from 0.6 to 63 at a constant pH 3.0 and 25°C [Fig. 6(a)]. At a fixed OH/CHO ratio of 14, reactions at pH 3 and 4 led to PVA hydrogels that swelled significantly higher (SD $\sim$ 62) than those (SD $\sim$ 23) at the lower pH of 1 and 2 [Fig. 6(b)]. However, reaction temperatures between 25 and 50°C had little effect on swelling of the hydrogels formed [Fig. 6(c)]. It should be noted, that hydrogels with SD greater than 40 were too soft to stay intact from handling. The hydrogels formed at pH $>$ 4 became soluble when immersed in water for 7 days. Therefore, pH 3 and 25°C were concluded to be the optimal reaction conditions for forming PVA gel on GA-activated cellulose.

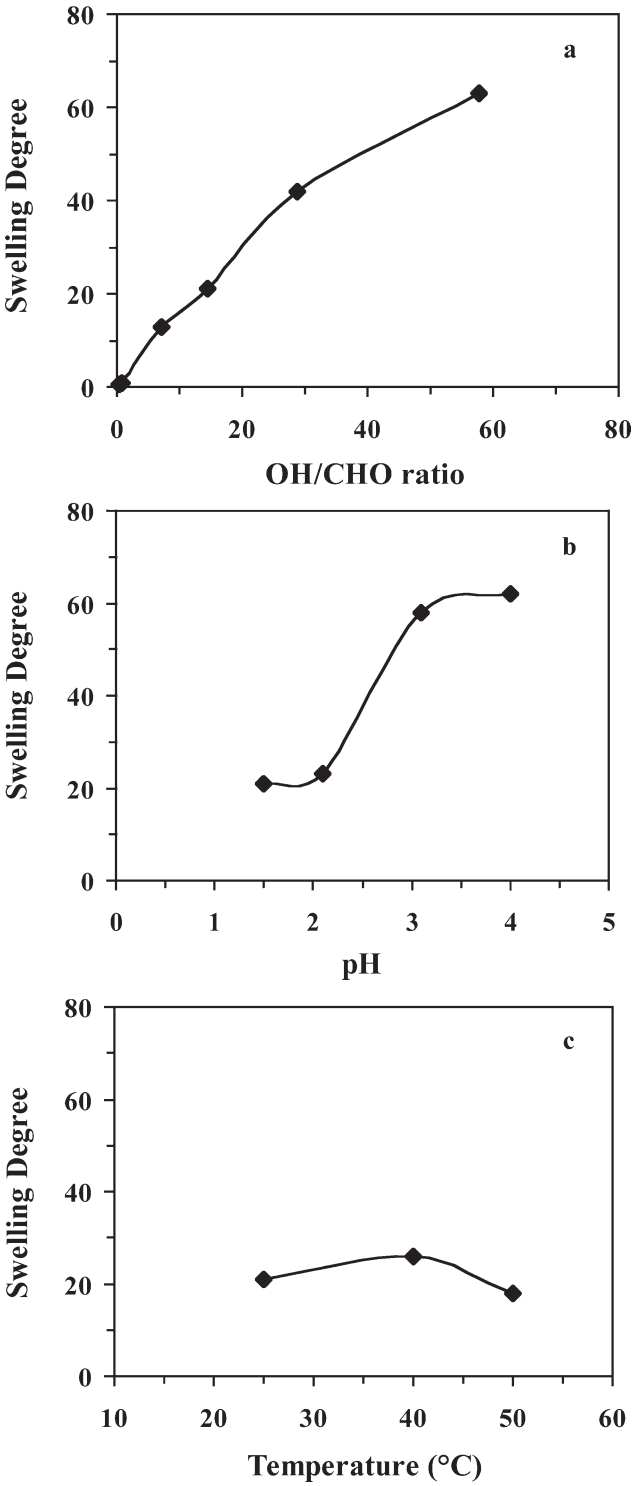
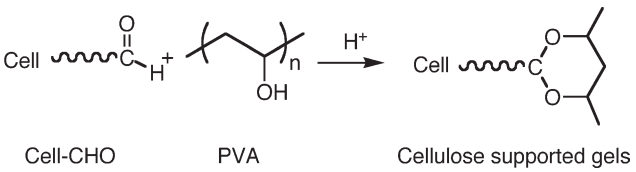


Figure 6 Crosslinking conditions on swelling degrees of PVA-GA gels: (a) OH/CHO molar ratios (ambient temperature and pH 3.0); (b) medium pH (OH/CHO of 14, ambient temperature; (c) temperature (OH/CHO of 14, pH 3.0).



Scheme 4 Cellulose fiber supported PVA hydrogel formation.

The GA-activated cellulose supports PVA hydrogel via reaction of the PVA hydroxyls with the free aldehydes on the cellulose fiber surfaces (Scheme 4). At a constant free aldehyde level, the swelling behavior of the PVA hydrogel can be controlled by the amount of PVA or the OH/CHO ratio. In other words, the higher OH/CHO the fewer bonds there are between the PVA and the cellulose surfaces. This explains the higher SD or the positive relationship between SD and the OH/CHO ratio. This process is simple and effective to chemically bond a water-soluble PVA to cellulose fiber surfaces to form hydrogels without the need for additional crosslinker.

CONCLUSIONS

Cellulose fibers and microcrystalline powders have been functionalized via reactions with difunctional GA and PEG diacylchloride to create aldehyde (Cell-CHO) and acylchloride (Cell-PEG—COCl) activated cellulose. On PEG diacylchloride reacted cellulose fibers, 0.24 mmol free COOH and 1.68 mmol OCO/COOH of per gram cellulose were generated. The free COOH attained was 14% of the total OCO/COOH. In microcrystalline powders (Cell-PEG—COCl), the free COOH generated were 40, 62, 50, and 12% of the total OCO/COOH at 0.5, 1, 2, and 20 COCl/OH ratios, respectively. The highest COCl of 0.37 mmol/g cellulose was produced from reaction at 1 COCl/OH ratio. These data showed that PEG-diacylchloride react more efficiently with MC cellulose powders than cellulose fibers. Furthermore, the generation of free COOH was optimized at the lower COCl/OH ratio where the tendency to form half-esters (pathway I) appeared higher than diesters.

Activating cellulose with GA was shown to improve with increasing GA concentrations and the free aldehyde reached 0.83 and 1.26 μmol/g cellulose for reactions at 8% and 18% GA, respectively. The reactivity of Cell-CHO was utilized to form cellulose supported PVA hydrogels on the GA-activated cellulose fiber surfaces. The swelling degree (SD) of the gels formed on cellulose fiber surfaces improved significantly with increasing OH/CHO ratios from 0.4 to 58 at pH 3.0 and 25°C. This surface activation coupled with reaction with PVA approach is simple and yet robust to chemically bond hydrogels on cellulose fiber surfaces without the need for additional crosslinking agents.

This activation approach is applicable to generate hydrogels from other water-soluble polymers on cellulose fibrous supports and is an efficient way to improve the physical and handling properties, as well as to expand the swelling properties of hydrogels. These cellulose fiber supported hydrogels could be excellent matrix for immobolization of enzymes, as we have demonstrated with electrospun PVA hydrogel fibers.[14] Furthermore, this approach demonstrates the potential of attaching other functional compounds and polymers that contain reactive groups toward aldehyde, i.e., primary and secondary amines, hydrazine, amino acids, peptides, and polyamino acids.

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